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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,210	01/14/2004	Se-Jin Lee	JHU1130-4	5556

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EXAMINER	
MERTZ, PREMA MARIA	
ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 08/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/758,210	LEE ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-21* is/are pending in the application.

4a) Of the above claim(s) *16-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,15 and 19-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/14/2004*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

Group 1. Claims 14-17, are drawn to a method for detecting a cell proliferative disorder *in vivo* using a GDF-7 antibody, classified in Class 514, subclass 2.

Group 2. Claims 14-15, 19-21, are drawn to a method for detecting a cell proliferative disorder *in vitro* using a GDF-7 antibody, classified in Class 435, subclass 7.1.

The inventions are distinct each from the other because of the following reasons:

Although there are no provisions under the section for "Relationship of Inventions" in M.P.E.P. 806.05 for inventive groups that are directed to different methods, restriction is deemed to be proper because these methods appear to constitute patentably distinct inventions for the following reasons: Groups I-II are directed to methods that are independent and distinct, each from the other, because the methods are practiced with materially different process steps, materially different starting materials and each method requires a non-coextensive search because of different starting materials and process steps.

Having shown that these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and recognized divergent subject matter as defined by MPEP § 808.02, the Examiner has *prima facie* shown a serious burden of search (see MPEP § 803). Therefore, an initial requirement of restriction for examination purposes as indicated is proper.

2. During a telephone conversation with Lisa A. Haile on 7/20/2005 a provisional election was made with traverse to prosecute the invention of Group II, claims 14-15, 19-21. Affirmation

of this election must be made by applicant in replying to this Office action. Claims 16-18 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. It is suggested that the title be amended to recite a method of detecting GDF-7 using a GDF-7 antibody.

4. Applicant is reminded of the proper content of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following:
(1) if a machine or apparatus, its organization and operation;
(2) if an article, its method of making;
(3) if a chemical compound, its identity and use;
(4) if a mixture, its ingredients;
(5) if a process, the steps.

Extensive mechanical and design details of apparatus should not be given.

The instant abstract fails to recite a method of using GDF-7 antibodies.

Appropriate correction is required.

Claim rejections-35 USC § 101

5. Claims 14-15, 19-21 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The instant application has provided a description of an isolated nucleic acid encoding a protein, growth differentiation factor-7 (GDF-7), and the protein encoded thereby. The instant application does not disclose the biological role of this protein or its significance.

It is clear from the instant specification that the instant protein (GDF-7) is an "orphan protein". This is a protein whose cDNA has been isolated because of its similarity to known proteins. In the instant case, the GDF-7 protein has been compared to other members of the TGF-β family (see Figure 3 and Brief Description of Drawings on page 4, lines 7-10). However, from a review of Figure 3, one of ordinary skill in the art would not be able to conclude that the GDF-7 protein of the instant invention is a member of the TGF-β superfamily because other than the conserved cysteine residues, Applicants have failed to disclose the degree of structural similarity between the instant GDF-7 protein and other members of the TGF-β superfamily and also there is no experimental data demonstrating the ability of the claimed protein to function as a member of the TGF-β superfamily.

The specification on page 5, lines 14-17, discloses that based on the known activities of many of the members of the TGF-β superfamily, it can be expected that GDF-7 will also possess biological activities that will make it useful as a diagnostic and therapeutic reagent. The specification on page 6, lines 7-9, also discloses that by analogy, GDF-7 "may" have applications in the treatment of neurodegenerative diseases or in maintaining cells or tissues in culture prior to transplantation. However, contrary to this assertion, the assertion that because

the TGF-β proteins of the prior art have utility, so the instant protein has utility does not hold because the Examiner is not disputing the utility of other proteins, but in the instant case, Applicants have failed to disclose a cause and effect condition of the instantly claimed protein based on evolutionary origin.

On page 14, lines 6-16, the instant specification discloses that the invention provides a method of detecting a cell proliferative disorder of neural tissue using a GDF-7 antibody. However, Applicants have failed to show in Figure 1, that there is differential expression of the mRNA encoding the GDF-7 protein in the different stages of fetal development and neonatal development and in the neuroblastoma cell line related to normal adult neural tissue i.e. Applicants have failed to show differential expression of the mRNA encoding the GDF-7 polypeptide in normal neural cells and in neural cells with a neural cell proliferative disorder.

There are thousands of house keeping genes expressed both in cancer and human cells. The employment of the antibody to the GDF-7 protein of the instant invention, in diagnostics to detect the presence of the GDF-7 protein in a cell proliferative disorder is not a substantial or specific utility, because a change in the expression of the protein has not shown to be associated with a disease or condition. All human proteins can invariably be classified into two categories, those which are expressed in a tissue or developmentally specific manner and those which are expressed ubiquitously. It can be alleged that any protein which is expressed in a tissue specific manner can be employed to detect the tissue in which it is expressed in a sample. Alternately, a human protein which is expressed ubiquitously can be employed to detect the presence of any human tissue in a sample.

In Figure 1 (page 4, lines 1-4) Applicants have described RNase protection assays for detecting the presence of GDF-7 mRNA in neural tissue and in immortalized neural cell lines. However, in Figure 1, there is no indication of the expression of GDF-7 in normal neural tissue i.e. there is no indication of the basal level, if any, of GDF-7 expression to provide a standard for interpreting the data.

Figure 1 describes the result of the RNase protection assay in neural cells, however, there is no indication of the expression of a constitutively expressed gene as a control to indicate that the amounts of mRNA added in each sample were equivalent. There is no lane in Figure 1 to indicate a normal standard neural tissue sample. Applicants have failed to show that a change in proliferation of neural cells, due to a neural disorder, for example, would result in a corresponding change in GDF-7 levels detected, using a GDF-7 antibody.

There is little doubt that after complete characterization, the instant method will probably be found to have a patentable utility. The uses of the antibody to the GDF-7 protein (pages 14-15) e.g. for detecting a cell proliferative disorder of neural tissue, in *in vitro* immunodiagnosis or immunotherapy, are not specific, substantial or credible utilities because Applicants have failed to disclose any nexus between the claimed antibody to the GDF-7 protein and these recited disorders. Furthermore, since the instant protein has not been shown to be a disease marker or to be involved in a physiological process that one would want to manipulate for clinical effect, the instant specification does not disclose a "real world" use for the claimed antibody to the GDF-7 protein, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. 101 as being useful. Furthermore, because the claimed invention is not supported by a specific asserted utility for the reasons set forth above, credibility cannot be ascertained.

The instant claims are drawn to an antibody to the GDF-7 protein, of as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the protein identified in the specification as GDF-7, the instant invention is incomplete. The GDF-7 protein is known to be structurally analogous to proteins of the TGF-β family (Figure 3). In the absence of knowledge of the biological significance of the GDF-7 protein, there is no immediately obvious "patentable" use for it. To employ an antibody to the GDF-7 protein of the instant invention in the detection of "cell proliferative disorders" as recited on page 13, lines 24-27 and page 14, lines 1-5, is clearly to use it as the object of further research which has been determined by the Courts to be a non-patentable utility. Since the instant specification does not disclose a "real world" use for the claimed antibody to the GDF-7 protein, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. 101 as being useful. Furthermore, because the claimed invention is not supported by a specific asserted utility for the reasons set forth above, credibility cannot be ascertained.

Furthermore, the instant claims are drawn to a method of using an antibody to a GDF-7 polypeptide, which has an as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the protein identified in the specification as having structural homology to members of the TGF-β family (page 5, lines 14-17), the instant invention is incomplete. The instant specification does not disclose any information regarding functional characteristics or the biological activity of the GDF-7 protein. The specification does not demonstrate that the GDF-7 polypeptide actually displays any of the activities of other TGF-β family members that are recited on page 5, lines 18-27 and page 6. In the absence of knowledge of the specific biological significance of the GDF-7 protein, there is no immediately

obvious patentable use for an antibody to GDF-7 in the claimed method. Since the instant specification does not disclose a "real world" use for the antibody to the GDF-7 protein in the claimed method, then the claimed invention is incomplete and, therefore, the method does not meet the requirements of 35 USC 101 as being useful.

A protein of unknown function would have utility if it can be employed as an indicator of a diseased state or of the presence of a disorder. Applicant is only required to identify one substantial credible utility and the employment of an antibody to the GDF-7 protein only as the subject of further research does not satisfy the utility requirement of 35 U.S.C. 101 because the courts have interpreted this statute as requiring an invention to have substantial utility where specific benefit exists in currently available form. The employment of an antibody to the GDF-7 protein of the instant invention, in a method of detecting cell proliferative disorder, is not a substantial or specific utility.

Applicants disclose in the specification that the claimed protein has homology to the TGF-β family of proteins (page 5, lines 12-17). The state of the art is such that functional information can be automatically derived from structural information only to a limited extent, (see Sklonick et al, Nature Biotechnology, Vol.18, No.3, pages 283-287, especially page 286, middle of column 1). Sklonick et al also state that knowledge of the overall structure or domain family is still not enough to confidently assign function to a protein. Therefore, there is little doubt that, after further characterization, the protein is found to be member of the TGF-β family, the claimed protein would have a specific, substantial and credible utility. However, further characterization is part of the invention and until it had been undertaken, the claimed invention is not supported by a specific asserted utility or a well established utility. The claimed invention is

directed to a method of using an antibody to a GDF-7 polypeptide of as yet undetermined function or biological significance and thus, the claimed invention is not supported by either a specific and substantially asserted utility or a well established utility.

Claims 14-15, 19-21, are also rejected under 35 U.S.C. 112, first paragraph, as failing to adequately teach how to use the instant invention. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4a. Claims 14-15, 19-21, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting in vitro, the presence of GDF-7 in a neural tissue sample by contacting an antibody to a GDF-7 polypeptide of amino acid sequence set forth in SEQ ID NO:6, does not reasonably provide enablement for a method of detecting a cell proliferative disorder using an antibody to GDF-7. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claim 14 recites "detecting a cell proliferative disorder", however, the specification is only enabling for a method for detecting in vitro the presence of GDF-7 in a sample using a GDF-7 antibody. Applicants have not taught how the difference in expression between GDF-7 between a specimen from a subject and a control sample is indicative of a cell proliferative disorder. The specification does not enable the detection of various cell proliferative disorders encompassed by the claims. Furthermore, the claim recites "cell proliferative disorders" but the specification does not disclose or provide guidance as to what these "cell proliferative disorders" are, which requires a great deal of guidance regarding interpreting the results obtained by the claimed method. The specification fails to provide sufficient guidance because it is unpredictable what the expression of GDF-7 in "cell proliferative disorders" is relative to a control sample. Furthermore, with respect to claim 14, the specification does not disclose or provide guidance as to what the abnormal expression of GDF-7 is. Without this guidance, it would require undue experimentation to practice the invention as claimed.

Claims 15, 19-21 are rejected under 35 U.S.C. § 112, first paragraph insofar as they are dependent on claim 14 for its limitations.

Claim Rejections - 35 USC § 112, second paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14-15, 19-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 is rejected as vague and indefinite for several reasons.

Claim 14 is rejected as vague and indefinite for reciting "cell proliferative disorder". The specification on page 13, lines 24-27, discloses that the term "cell proliferative disorder" encompasses malignant as well as non-malignant cells. Therefore, it is unclear what the metes and bounds of the term are with respect to non-malignant cells. Does the term also encompass HIV infections in which T-cells are affected or inflammatory conditions in which monocytes and macrophages are involved?

Claim 14 is rejected as vague and indefinite for reciting "a fragment thereof". The metes and bounds of the term are unclear because a fragment can encompass a single amino acid. It is suggested that the claim be amended to recite the size of the fragment for which there is a basis in the instant specification.

Claim 14 is vague and indefinite for reciting "a subject suspected of having a GDF-7 associated disorder". The specification on page 14, lines 14-16, discloses that the level of GDF-7 in a suspect cell can be compared with the level in a normal cell to determine whether the subject has a GDF-7 associated cell proliferative disorder. However, it is unclear what the characteristics of this "suspect cell" would be.

Claim 14 is vague and indefinite because the claim fails to recite steps. It is unclear from the claim what the result of binding of the antibody to the GDF-7 protein would be an indication of.

Claims 15, 19-21 are rejected as vague and indefinite insofar as they depend upon the above rejected claims for their limitations.

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (571) 272-0829.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prema Mertz

Prema Mertz Ph.D.
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Art Unit 1646
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